PQM Report on Evaluation of Laboratory Quality Management System: Medicine Quality Control Laboratory of the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA)

Bogotá, Colombia
October 11 - 15, 2010

Trip Report

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Executive Summary*

The objective of this trip was to perform an evaluation of the Quality Management System (QMS) of the medicine Quality Control (QC) of the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA).

The evaluation was performed using the following internationally recognized standards:

- WHO Good Practices for National Pharmaceutical Control Laboratories (GPPQCL) (Technical Report Series, No. 957, 2010, Annex 1, also referred to as WHO Good Laboratory Practices or "GLP") and,
- The International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) 17025:2005 Standards

The ultimate goal for the medicine QC laboratory of INVIMA is to obtain ISO/IEC 17025:2005 accreditation and subsequently be incorporated in the list of World Health Organization (WHO) Prequalified (PQ) medicine QC laboratories.

The evaluation was performed by PQM and a representative from the Comisión para el Control de Calidad de Medicamentos (CCCM) de Uruguay, a WHO PQ lab.

The following are the key findings and conclusions:

- INVIMA is committing significant financial and human resources towards implementing a QMS that is based on ISO/IEC 17025:2005 for all of the QC laboratories.
- The medicine QC laboratory has made significant progress in implementing a QMS that is compliant with ISO/IEC 17025:2005 and WHO GPPQCL.
- Nonetheless, the evaluation did identify significant nonconformities with both ISO/IEC 17025:2005 and WHO GPPQCL standards.
- The medicine QC laboratory of INVIMA is not ready for a formal ISO/IEC 17025:2005 assessment or WHO inspection.

PQM has provided details of the nonconformities identified, including suggested corrective action(s), and suggested timelines to remediate the nonconformities.

INVIMA will work on implementing corrective actions and continue to strengthen their QMS. PQM and/or CCM will schedule a follow-up visit in approximately 6 months.

* This section will be translated into Spanish and disseminated separately to country partners.

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About PQM

The Promoting the Quality of Medicines (PQM) program, funded by the U.S. Agency for International Development (USAID), is the successor of the Drug Quality and Information (DQI) program implemented by the United States Pharmacopeia (USP). PQM is USAID's response to the growing challenge posed by the proliferation of counterfeit and substandard medicines. By providing technical assistance to developing countries, PQM helps build local capacity in medicine quality assurance systems, increase the supply of quality medicines to priority USAID health programs, and ensure the quality and safety of medicines globally. This document does not necessarily represent the views or opinions of USAID or the United States Government. It may be reproduced if credit is given to PQM and USP.

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- CCCM, in particular, Q.F. Monica Hirschhorn, for providing assistance to PQM-sponsored activities
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ACRONYMS

AMI	Amazon Malaria Initiative
CA	Central America
CAPA	Corrective and Preventive Action
DQI	Drug Quality and Information Program
EOI	Expression of Interest
GLP	Good Laboratory Practices
GPPQCL	Good Practices for Pharmaceutical Quality Control Laboratories
IAAC	Inter American Accreditation Cooperation
IEC	International Electrotechnical Commission
ILAC	International Laboratory Accreditation Cooperation
ISO	International Organization for Standardization
LAC	Latin America and Caribbean
LIF	Laboratory Information File
MRA	Medicine Regulatory Authority
OMCL	Official Medicines Control Laboratory
PAHO	Pan American Health Organization
PQ	Prequalification
PQM	Promoting the Quality of Medicines Program
QA	Quality Assurance
QC	Quality Control
QM	Quality Manual
QMS	Quality Management System
SOP	Standard Operating Procedure
USAID	United States Agency for International Development
USP	United States Pharmacopeia
WHO	World Health Organization

Background*

Since 2002, the U.S. Agency for International Development (USAID) has supported U.S. Pharmacopeia (USP) participation—first through the Drug Quality and Information program and, currently, through the Promoting the Quality of Medicines (PQM) program—in the Amazon Malaria Initiative (AMI). Within the context of AMI, PQM has collaborated with the countries to strengthen their Quality Assurance Systems. In Colombia, PQM has worked mainly in three areas: (a) Supporting the National Malaria Control Program (NMCP) to establish Medicine Quality Monitoring (MQM) activities in sentinel sites through the use of basic tests; (b) Developing a Manual of Procedures for the Integral Management of the Supply of Malaria Medicines that integrates the three-level approach for quality control (QC) throughout the supply chain; and (c) Strengthening testing capabilities and the Quality Management System of the Official Medicine Control Laboratory (OMCL) of the Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA), Colombia's Medicine Regulatory Authority (MRA).

On this visit, PQM was accompanied by staff from the Comisión para el Control de Calidad de Medicamentos (CCCM) de Uruguay. In September 2010, CCCM was added to the World Health Organization (WHO) list of prequalified (PQ) QC laboratories. Based on these credentials, CCCM agreed to assist PQM in evaluating the QMS of INVIMAS's medicine QC laboratory and provide recommended corrective actions to ensure compliance with international quality standards.

Purpose of Trip*

This purpose of the trip was to evaluate the QMS of the medicine QC laboratory of INVIMA.

Overview of Activities*

The goal for the medicine QC laboratory of INVIMA is to obtain ISO/IEC 17025:2005 accreditation and subsequently be incorporated in the list of WHO Prequalified medicine QC laboratories. Attaining working conditions that conform to these stringent standards will assure that the administrative and technical operations of the laboratory are functioning at the highest internationally recognized standards and will provide Colombia's Ministry of Health, especially INVIMA — Colombia's MRA—with a QC laboratory capable of producing reliable, accurate and valid results.

For details of other meetings with partners during this time, see Annex 1.

* This section will be translated into Spanish and disseminated separately to country partners.

Item	Description
Institution Evaluated	Medicine QC Laboratory of INVIMA Bogotá, Colombia
Specific Objectives	The intent of this visit was to evaluate the QMS of the medicine QC laboratory of INVIMA utilizing the following standards: o WHO Good Practices for National Pharmaceutical Control Laboratories (GPPQCL) (Technical Report Series, No. 957, 2010, Annex 1, also referred to as WHO Good Laboratory Practices or "GLP") and, o The International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) 17025:2005 Standards Increase the capacity of laboratory staff regarding: o Processes involved with ISO/IEC 17025:2005 accreditation and WHO PQ o Internal auditing techniques o External audit expectations
Partners	• INVIMA • CCCM • PQM
Evaluators	• Adrian Barojas, PQM • Monica Hirschhorn, CCCM
Key Personnel	• See Annex 2 for List of Participants • See Annex 3 for the participants' evaluations (in Spanish)
Agenda	See Annex 4 for a detailed Agenda
Areas Evaluated	• QMS Documents, focusing on quality manual & critical SOPs • Accommodations (Premises) • Handling of test items • Document and record control • Equipment • Staff training • Test methods • Reporting of results • Safety procedures See Annex 5 for details
Key Findings	• INVIMA is committing significant financial and human resources towards implementing a QMS that is based on ISO/IEC 17025:2005 for all of the QC laboratories. • The medicine QC laboratory has made significant progress in implementing a QMS that is compliant with ISO/IEC 17025:2005 and WHO GPPQCL. • The medicine QC laboratory has narrowed their scope to include 7 tests for their initial accreditation: o 4 for physico-chemical testing (HPLC, UV, TLC & Dissolution) o 3 for microbiological testing (LAL, sterility & microbiological limit) • The evaluation did identify significant nonconformities with both ISO/IEC 17025:2005 and WHO GPPQCL standards.

	• PQM and CCCM identified 14 nonconformities: o 10 Major (MAJ) o 3 Minor (MIN) o 1 Opportunity for Improvement (OFI) For additional details and recommended corrective actions see Annex 5.
Conclusion	The medicine QC laboratory of INVIMA is not ready for a formal ISO/IEC 17025:2005 assessment or WHO inspection.
Next Steps	• The medicine QC laboratory should perform the following activities to improve their QMS: o Continue to implement their Quality Plan and modify it accordingly to ensure the observations received during this evaluation are adequately addressed. o Perform internal audits of the areas not covered by this evaluation and ensure the audits are performed with sufficient rigor. o Communicate with PQM and CCCM regarding any requests for technical assistance in implementing their Quality Plan. • Communicate with the national accrediting body (Organismo Nacional de Acreditación de Colombia – ONAC) to obtain clarification of when ONAC is expected to receive international recognition for accrediting testing laboratories. o If ONAC is not expected to receive international recognition, PQM recommends the medicine QC laboratory of INVIMA engage another accrediting body that does have international recognition. This will maximize the financial and human resources utilized to implement a QMS that is complaint with ISO/IEC 17025:2005. • Schedule a follow-up evaluation with PQM and CCCM in approximately 6 months.

Annex 1

PQM Visit: Additional Meetings*

Meeting with Sub-Director of Medicines and Biological Products, INVIMA

October 14, 2010
Participants: See *Annex 2* for a complete list of participants.

Meeting Proceedings and Conclusions:

PQM discussed the objectives and main findings of the current trip with the sub-director, particularly the need for her continuous commitment to improve the QMS. The sub-director committed to providing her staff with the necessary support to implement a QMS that is compliant with both WHO GPPQCL and ISO/IEC.

PQM also stressed the need for INVIMA to communicate with the national accrediting body (ONAC) to obtain clarification of when ONAC is expected to receive international recognition for accrediting testing laboratories. If ONAC is not expected to receive international recognition, PQM recommends the medicine QC laboratory of INVIMA engage another accrediting body that does have international recognition. This will maximize the financial and human resources utilized to implement a QMS that is complaint with ISO/IEC 17025:2005. The sub-director agreed that INVIMA must perform due diligence regarding finding an appropriate accrediting body that will allow the laboratory to obtain maximum recognition for their future accreditation.

Additionally, PQM and CCCM expressed their willingness to provide technical assistance and perform follow-up visits as necessary to assist INVIMA's medicine QC laboratory in improving their QMS.

Next Steps

- PQM and CCCM will work with the medicine QC lab of INVIMA to address the observations identified during the evaluation (See *Annex 5*).

Meeting with USAID/Colombia

October 14, 2010
Participants: See *Annex 2* for a complete list of participants.

Meeting Proceedings and Conclusions:

PQM discussed the objectives and main findings of the current trip and other AMI funded activities being implemented in-country with USAID/Colombia. USAID/Colombia requested that PQM keep the Mission updated on any USAID-funded initiatives.

Next Steps

- PQM will update USAID/Colombia as activities continue to develop.

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Annex 2

PQM Meetings: Lists of Participants

Bogotá, Colombia

October 11 - 15, 2010

October 11, 12 & 15 – Presentations

Participant	Institution
Eduardo Vergel Bayona	INVIMA
Efrén Bohórquez Ortega	INVIMA
Gina Alejandra Díaz Bernal	INVIMA
Pablo César Rincón Rincón	INVIMA
Luis Hernán Ricardo Enciso	INVIMA
Gregorio Torres Rangel	INVIMA
Sofía Isabel Laverde Manotas	INVIMA
Adriana Ortiz Valderrama	INVIMA
Álvaro Gómez sarmiento	INVIMA
Flor Alix Umaña Cardozo	INVIMA
Alba Marina Fernández Sánchez	INVIMA
María Fernanda de la Ossa	INVIMA
Fanny Trujillo González	INVIMA
Leidy Carolina Rodríguez Morales	INVIMA
Diana Cristina Charry Vargas	INVIMA
Jenny Paola Zarate Jiménez	INVIMA
Deisy Magnolia Lozano Torres	INVIMA
Martha Inés Rincón	INVIMA
Patricia León Triviño	INVIMA
Ney Callas Cantillo	INVIMA
Catalina Pardo Benavides	INVIMA
Belsy Tibaduiza rodríguez	INVIMA
Beatriz Fierro Rivera	INVIMA
Mauricio Prieto Moya	INVIMA
Flor Leguizamón Palacio	INVIMA
Mabel Constanza Barbosa Romero	INVIMA
Edna Carime Díaz Sanabria	INVIMA
Delia Giraldo	INVIMA
Monica Hirschhorn	CCCM
Adrian Barojas	PQM

October 12 - 14, 2010 – INVIMA QMS Evaluation

Participant	Institution
Eduardo Vergel Bayona	INVIMA
Efrén Bohórquez Ortega	INVIMA
Gina Alejandra Díaz Bernal	INVIMA
Pablo César Rincón Rincón	INVIMA
Fanny Trujillo González	INVIMA

Leidy Carolina Rodríguez M.	INVIMA
Catalina Pardo Benavides	INVIMA
Monica Hirschhorn	CCCM
Adrian Barojas	PQM

October 14, 2010 – Meeting with INVIMA Sub-Director of Medicines and Biological Products

Participant	**Institution**
Marta Rodriguez	INVIMA
Fanny Trujillo González	INVIMA
Eduardo Vergel Bayona	INVIMA
Pablo César Rincón Rincón	INVIMA
Monica Hirschhorn	CCCM
Adrian Barojas	PQM

October 14, 2010 – Meeting with USAID/Colombia

Participant	**Institution**
Thea Villate	USAID/Colombia
Adrian Barojas	PQM

Annex 3

Evaluación por los Participantes

Fecha de Evaluación del Laboratorio: 11 - 15 de Octubre del 2010

En base a las actividades llevadas a cabo durante la evaluación del laboratorio, incluyendo material educativo y otras actividades asociadas, se solicita que complete el siguiente formulario en todos los las categorías indicadas.

[*Por favor complete y devuelva al instructor/facilitador después de finalizadas todas las actividades de evaluación*]

Indicador	Coincido completamente	Coincido en parte	No coincido
1. Los objetivos del curso fueron relevantes a mis actividades	22		
2. El curso satisfizo mis expectativas	22		
3. El material presentado fue accesible	22		
4. El material presentado fue de utilidad y contribuirá a mi desempeño en el trabajo	22		
5. Hubo un número suficiente de ejercicios prácticos para facilitar el entendimiento de la evaluación	20	2	
6. El tiempo dedicado a las sesiones fue apropiado para el material necesario para la evaluación	21	1	
7. Los instructores tenían conocimiento del tema	22		
8. Los instructores permitieron un nivel apropiado de participación de los asistentes a las clases	22		

Otros comentarios/Sugerencias:

1. ¿Qué tópico(s) o aspectos no deberían incluirse en la evaluación en un futuro?

- La gran mayoría de los participantes indicaron satisfacción con los diferentes aspectos de la evaluación

2. ¿Cuáles son sus recomendaciones/sugerencias para mejorar la evaluación?

- Incrementar el tiempo de la evaluación (2)
- Realizar la evaluación con expertos en el área de microbiología (2)
- Incrementar ejercicios prácticos de auditorías, particularmente para los auditores internos (1)
- Incorporar mas capacitación para el personal auxiliar del laboratorio (1)
- Incrementar la frecuencia de visitas de PQM y CCCM (1)

- Asegurar que la evaluación cubre todos los elementos (clausulas) de las normas (2)

3. ¿Qué es lo que más le gustó de la evaluación?

- La dedicación, objetividad y el conocimiento de los instructores (8)
- El detalle y la rigurosidad de la evaluación (6)
- El apoyo en mejorar deficiencias del sistema y en dar sugerencias inmediatas para remediar no-conformidades (4)
- Discusiones de ejemplos de otros laboratorios de la región (4)
- El enfoque educativo de las charlas (3)

4. Describa en qué temas o actividades le gustaría recibir apoyo en el futuro:

- Seguimiento por PQM y CCCM a las no-conformidades observadas durante la evaluación (3)
- Incertidumbre (3)
- Verificación de métodos (3)
- Validación de métodos (3)
- Fundamentos de metrología (3)
- Capacitaciones prácticas para el personal del laboratorio en métodos microbiológicos (3)
- Verificación/calificación de equipos (2)
- Interpretación de capítulos generales, advertencias generales y monografías de la USP y otras farmacopeas (2)
- Metodología y análisis de datos (1)
- Incrementar el tiempo para apoyar en las mismas actividades cubiertas durante esta evaluación (1)
- Visitar a otros laboratorios de la región para observar como implementan sus SGC (1)
- Realizar una evaluación exclusivamente para el laboratorio de microbiología (1)
- Apoyar en obtener infraestructura que asegura los resultados emitidos por el laboratorio son confiables (1)
- Incrementar la interacción con otros laboratorios de la región (1)
- Asegurar que se mantengan abiertas vías de comunicación con los facilitadores (1)
- Apoyo en desarrollar formatos de informes (1)
- Apoyo en desarrollar procedimientos para la selección de proveedores de buena calidad (1)

Annex 4

Medicine QC Laboratory of INVIMA QMS Evaluation: Agenda*

Bogotá, Colombia
October 11 - 15, 2010

Monday, October 11:
- Tour of laboratory Installations
- Presentation: Introduction and Objective of Evaluation
- Presentation: International Quality Standards & OMCL Situation in Americas
- Presentation: Implementing a Rigorous Quality Management System
- Presentation: CCCM Experiences

Tuesday, October 12:
- Presentation: Expectations of External Audits & Recommended Auditee Behavior
- Presentation: Simulated Method Audit
- Begin Facility Inspection (Performed by Monica Hirschhorn - CCCM)
- Begin Process Audit (Performed by Adrian Barojas – PQM)

Wednesday, October 13:
- Continue PQM Facility inspection
- Continue Process Audit

Thursday, October 14:
- Finish PQM Facility inspection
- Finish Process Audit
- Meeting with INVIMA Sub-director of Medicines and Biological Products
- Meeting with USAID/Colombia

Friday, October 15:
- Presentation: Evaluation Findings, Recommendations, and Next Steps
- USP/NF Question and Answer Session

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Annex 5

Details of PQM and CCCM Evaluation*

Medicine QC Laboratory of INVIMA
Bogotá, Colombia
October 11 – 15, 2010

Areas Covered and Focus of Evaluation:

The evaluation focused on the following areas:

- Improve management and staff understanding of WHO GPPQCL and ISO/IEC 17025:2005 standards
- Build capacity in internal auditing procedures (process, facility and method audits)
- Review laboratory infrastructure
- Review components of the QMS:
    - Key documents, specifically the Quality Manual (QM) and critical Standard Operating Procedures (SOPs)
    - Sample handling procedures
    - Document Control System (DCS)
    - Staff training records
    - Laboratory notebooks
    - Equipment records, maintenance and calibration program
    - Equipment records and logbooks
    - Test methods
    - Reporting of results
- Review safety procedures
- Identify areas to streamline work processes

Key Findings:

It is evident that the medicine QC laboratory of INVIMA dedicates substantial resources to ensuring the lab's results are valid and reliable. The following are some noteworthy characteristics of the current QMS and the lab's commitment to quality:

- The technical capacity of the laboratory is excellent and the staff clearly displays a willingness to identify their deficiencies and improve the quality of their services.
- The laboratory has all of the necessary equipment to effectively perform QC analysis according to compendial methods.
- While there are some deficiencies in the lab infrastructure (discussed below), the overall infrastructure is adequate to perform QC analysis according to international quality standards.
- Each laboratory (medicine physicochemical and microbiological) has a designated staff (facilitador de calidad) that performs QA functions and implements the QMS, which allows the laboratory to establish a stringent QMS across all of the pertinent laboratories.

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It is important to note that communication across departments (between the facilitadores de calidad) will be of utmost importance.

- Currently, INVIMA as a whole institution, which includes the medicine QC lab, is undergoing the process of implementing GP 1000 standards (the national equivalent of ISO 9011:2008). As a result the medicine laboratory has a QMS with a good foundation that will allow a smooth transition to ISO/IEC 17025:2005 standards.
    - Note: Subsequent to this visit, INVIMA underwent an audit for this standard.
- Generally speaking the QMS documents of the medicine QC lab are satisfactory; however, implementation of these documents remains a critical challenge. The following highlight some of the strengths of the medicine QC laboratory QMS documentation:
    - An advanced QMS with the following components:
        - Well defined Quality Policy (QP)
        - Clearly defined scope for the QMS that covers all operations
        - QMS with well-defined objectives and structure
    - DCS that is adequately controlled and managed by the designated staff. The DCS includes:
        - Procedures for the creation, revision, release, and distribution of all the documents
        - A master list of controlled documents, including SOPs
    - Staff functions and requirements
    - Equipment requirements, including validation and calibration program
    - Sample handling procedures
    - Record control procedures
    - Internal audit procedures
    - CAPA procedures

The presence and characteristics of these components are indicative of the significant financial and human resources that have been committed to improving the quality of the services provided by the medicine QC laboratory of INVIMA. It is important to acknowledge these achievements as they demonstrate consistent managerial support and proper execution by key lab staff.

Nonetheless, the evaluation did identify significant nonconformities with both WHO GPPQCL and ISO/IEC 17025:2005 standards.

Overview of Evaluation Observations[†]:

No	Severity of Non-conformity (MAJ, MIN, OFI)	Area of Evaluation	ISO/IEC 17025:2005 Clause	WHO GPPQCL Clause
1	MAJ	Accommodations (Premises) & Handling of Test Items	5.3.1, 5.8.1 & 5.8.4	7.10, 14.9 & 14.12
2	MAJ	Personnel	5.2.1	6.2
3	MAJ	Quality Management System	4.2.1	2.1
4	MAJ	Quality Management System	4.2.1	2.1 & 2.2
5	MAJ	Control of Records	4.13.2.1	4.2
6	MAJ	Test Methods	5.4.1 & 5.4.2	16.5 & 17.3
7	MAJ	Accommodations (Premises)	5.3.2 - 4	7.3 & 7.7
8	MAJ	Equipment	5.5.2, 5.5.5 & 5.5.8	8.3, 12.2 – 6 & 12.8
9	MAJ	Uncertainty of Measurement	5.4.6.1 - 3	18.10
10	MAJ	Monitoring of Environment & Control of Nonconforming Work	4.9 & 5.3.2	7.3
11	MIN	Safety	NA	21.2 & 21.3
12	MIN	Supplier Evaluation	4.6.4	9.2
13	MIN	Storage of Documents & Records	4.13.1.2	7.5
14	OFI	Reporting of Results	5.10.2.k & 5.10.2 – Note 2	18.11

For details of each observation, evidence, suggested corrective action(s), and suggested timeline, please refer to the individual sheet for the indentified observation.

This annex contains 14 individual observation sheets.

[†]The reported observations are a result of the sample of the QMS that was evaluated during the visit. To effectively implement a stringent QMS the lab should ensure the reported observations are not present in all areas of the QMS. It is important to note that similar observations may also occur or may be absent in other areas not included during the evaluation.

Additional Recommendations:

The following are additional recommendations that will allow the medicine QC lab of INVIMA to improve their efficiency and their compliance with WHO WPPQCL and ISO/IEC 17025:2005 standards.

- Include in the internal audit SOP checklists that will allow the internal auditors to ensure all areas of the QMS are covered. It is recommended to develop one checklist and indicate the relevant clauses for each standard (WHO GPPQCL and ISO/IEC 17025:2005). The checklist can be attached as annexes in the SOP.
- Begin tracking the elapsed time from the moment the sample is received and approved until the emission of the certificate of analysis (COA). This will allow the lab to monitor their efficiency and report progress as the QMS continues to be implemented and improve testing efficiency.
- Develop a record of the hardware available at the medicine QC laboratory. Currently this record is located at another INVIMA department and there are no records in the medicine QC laboratory.
- Develop validated and controlled excel worksheets for performing automated calculations for select tests (ex: HPLC, Dissolution, UV, KF, etc.). Once these sheets have been validated and are controlled properly they will increase efficiency by streamlining the calculation component of the selected tests.
- The format of sheets used to record daily use of equipment (logbooks) should include the acceptable range for the relevant specifications (ex: temperature: 8 - 15 C° for storing materials under "cool" conditions – per USP requirements). Adding this information will provide a rapid reference to analysts and allow them to decide if the operating conditions of the equipment are within the acceptable range; thus, indicating the equipment is adequate for use.
- Improve the labeling in the laboratory. For example add labels that clearly identify the storage areas for cooled standards and samples. This will ensure storage areas are adequately marked and help analysts store samples and standards in the appropriate areas.
- It is recommended to use more advanced thermometers to monitor the temperature of the facilities (cold room, testing areas, other storage areas, etc…). Currently in some areas, the lab (ex: sample storage room freezer: code EQ-FQ-038, in-process sample storage freezer: code EQ-FQ-036, medium storage freezer: INVIMA inventory code 07574), takes the temperature once a day and records this data. There is no continuous monitoring of the environment to see if there is a deviation from the relevant temperature specifications. The lab can either obtain a data-logger that performs continuous monitoring of the temperature or could obtain a thermometer that captures the maximum and minimum temperatures throughout the day. Improving the type of environmental monitoring will ensure the lab's facilities, including storage areas, do not deviate from the relevant specifications and potentially impact the quality of test results.
- Perform a back-up of the Excel file with the information indicating the storage location of left-over samples that have already been tested. Performing a back-up of this file will ensure that in the event of any issues with the original file there is a back-up and this valuable information is not lost.

- Perform in-house calibrations of thermometers against calibrated thermometers that are traceable to SI units. This is a more economic approach to ensuring all relevant temperature readings are performed with appropriate metrological traceability.
- Add the internal code for each reference standard to the corresponding CoA. Adding this information to the CoA will allow the lab to easily search and find CoAs when needed; thus, ensuring traceability of tests is maintained.
- Standardize equipment calibration/maintenance stickers. The stickers available on the equipment vary by service provider and in some instances do not indicate the due date for the next calibration/maintenance. Creating a standard format will reduce analyst confusion.
- Remove obsolete calibration/maintenance stickers from equipment. This will reduce the risk of an analyst recording the incorrect calibration/maintenance dates. Additionally, this can prevent analysts from deciding not to use equipment because they perceived the calibration/maintenance date had expired, when in reality the equipment is fit for use.
- Ensure that all signatures are accompanied with the respective date.
- Prepare reference standard solutions in duplicate. This will increase the reproducibility and validity of testing results, particularly in the microbiology lab.

PQM and CCCM are available to assist INVIMA's medicine QC laboratory in implementing the appropriate CAPAs and work towards improving the current QMS and ensure compliance with stringent internationally recognized quality standards. Additionally, the laboratory should use all additional available resources, specifically, the Pan American Network on Drug Regulatory Harmonization (PANDRH) GLP Working Group (WG), PAHO's THR/EM Project, and other regional OMCLs who are more advanced in their compliance with international standards. These three mechanisms can provide substantial technical assistance to help the laboratory obtain the desired accreditations.

PQM Evaluation Observations

Medicine QC Laboratory of INVIMA
Bogotá, Colombia
October 11 – 15, 2010

Reference Information	
Observation # 1	1 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Accommodations (Premises) & Handling of Test Items
ISO/IEC 17025:2005 Clause	5.3.1, 5.8.1, 5.8.2 & 5.8.4
WHO GPPQCL Clause	7.10, 14.9 & 14.12

Observation Details

Sample handling procedures pose a risk to the deterioration, loss, confusion and damage of the testing samples and can adversely affect the integrity and quality of the testing results.

Objective Evidence

The following highlight the lab's deficiencies with the handling of tests items:

1. A sample was found in the managerial offices (currently utilized as the sample receipt location) that had not been registered into the system. The sample was not coded with a unique number and it was not stored in a location that ensured restricted access and appropriate environmental conditions.
2. Samples that were in-process of being analyzed were stored (both physico-chemical and microbiological labs) in conditions without environmental controls.
3. Left-over samples that were to be returned to clients were found on the ground in the sample storage area in the physico-chemical lab.
4. The sample storage facilities and all the testing facilities (for both physico-chemical and microbiological) do not have established (in quality manual, SOPs or other documentation) specific criteria for what constitutes adequate environmental specifications (temperature and humidity).

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. While the laboratory does need to make some changes to the SOPs for how to handle samples (PO03-RM-602-P001 & PM03-CCP-PR03); they do provide a standardized procedure for sample handling. One of the reasons this issue occurs is that sample receipt is being performed at the

managerial office and it is a function better suited for the storage area. Regardless of where the samples are received it is critical for the lab to ensure all samples are immediately introduced into the system and are not placed aside. Priority must be given to ensure all samples are handled accordingly to ensure the integrity and quality of results are not compromised.

2. The laboratory should include in the relevant SOPs for environmental control and monitoring (for both the storage and testing areas) specific criteria for what constitutes adequate environmental specifications to ensure the testing results are not affected.

Suggested Timeline
Address this nonconformity within 1 – 2 months.

Reference Information	
Observation # 2	2 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Personnel
ISO/IEC 17025:2005 Clause	5.2.1
WHO GPPQCL Clause	6.2

Observation Details

There is a lack of evidence to prove lab analysts and staff have been trained properly prior to testing samples and monitoring the lab's environmental conditions.

Objective Evidence

The following are the major deficiencies, particularly as related to staff training records:

1. The records for the analyst (Sofia Isabel) performing test s for sample ID # 19425 had the following deficiencies:
    a. Training records did not match the minimum requirements indicated in the respective position description. The analysts did not meet requirements for minimum professional experience prior to being hired.
    b. Training records do not contain sufficient information. For example, the training record (PA03-GP-402/3-F001 from 30 Jun 10) for the use of Balance EQ-FQ-0006 does not include sufficient detail (no reference to specific SOP/method included in training) to ensure the analyst has been trained on the relevant equipment SOP.
2. The staff in charge of storage facilities (María Fernanda) has not been trained (there are no records) on the use of environmental monitoring equipment (data-loggers).
3. Staff is being trained on SOPs after the SOP date of approval/implementation. The following are examples of this issue:
    a. The SOP on how to perform HPLC analysis (PO04-DS-602-P002) was implemented on 31 Aug 09 and the training for Sofia Isabel was performed on 03 Dec 09, 3 months after the SOP was approved and implemented.
    b. The same issue was identified for all of the relevant staff training records for sample ID # 19903.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Develop and update job descriptions with sufficient flexibility in the minimum requirements. This will ensure the lab is capable of hiring staff that meet their technical requirements and at the same

time do not cause non-conformities due to variances in the description and staff records.

2. Ensure all training records provide sufficient detail. For example, the training Balance EQ-FQ-0006 should clarify what SOP/method was utilized during the training.

3. Update the document control and revision SOP and allocate time to train staff before an authorized SOP is implemented. This will ensure staff has sufficient time to become trained prior to implementing the SOP. The following is recommended:
    a. Ensure the document control and revision SOP explicitly states a training period will be observed between the document approval/dissemination and implementation.
    b. The time allotted for staff training should be established depending on the complexity of the task. In some instances documenting that staff have read and understood the new/revised SOP will suffice; however, more complex procedures will require hands-on training.
    c. The updated document control and revision SOP should also clearly indicate that adequate records of the training are necessary.
4. It is recommended to develop an overview (index) of all training activities (internal and external) for each staff. This will allow the lab to ensure all staff training records are updated and complete.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 3	3 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Quality Management System
ISO/IEC 17025:2005 Clause	4.2.1
WHO GPPQCL Clause	2.1

Observation Details
The lab's personnel do not effectively implement the QMS documents.

Objective Evidence
The following are examples of deficiencies in implementation of QMS documents, particularly SOPs: 1. Inconsistencies between staff implementation and the instructions in SOP (PAO6-GM-602-I016) on use of balances: a. The SOP indicates that daily verifications will be performed with calibrated weights (10 mg, 50 mg, 100 mg, 1 g & 10g); however, the equipment logbook (PAO6-GM-602-F0011) from 19 Aug 10 indicates the daily verification was performed with weights that is inconsistent with the SOP requirements (5g & 10g). b. The SOP states the acceptance criteria for each weighing is +/- 0.2 mg. The equipment logbook (PAO6-GM-602-F0011) from 19 Aug 10 indicates weights that are outside of the acceptance criteria indicated in the SOP (5g = 5.0003 g & 10 g = 10.0004 g). c. Staff cleaning practices after use is not consistent with the SOP. Balance, code EQ-FQ-006, was found with a white power in the weighing compartment. 2. Inconsistencies between staff implementation and the instructions in SOPs (POO4-DS-602-P003 & POO4-DS-602-F001) on use of laboratory datasheets/notebooks and reagent/solution labels. The SOP indicates that any modifications are to be performed by crossing out (with a single line) the relevant information and the analyst will include a justification and add initials and date. The following are examples of nonconformities with the internal SOPs: a. Notebook # 06-2010, Page 1184 b. Notebook # 0602-2010, Pages 373 -376 c. Labels of the following reagents/solutions did not follow the internal SOP for making changes/modifications: i. 4.8 N HCl ii. 4N HNO_3 3. Inconsistencies between the sample workflow SOP (PM03-CCP-PR03), the relevant SOPs that detail each stage (ex: SOP for sample receipt, storage, testing, etc…) and the actual processes being implemented in the lab. For example, there are inconsistencies between the lab's SOPs and the actual processes for the assignment of sample to analyst and revision of the draft of the CoA.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Ensure all new SOPs and SOP revisions adequately capture the actual processes being performed in the lab. It is imperative for the lab's SOPs to reflect the reality of the testing activities performed by the analysts. 2. Implement Corrective Action #2, with particular emphasis on ensuring lab staff are properly training on relevant QMS documents, particularly SOPs. 3. Increase frequency of internal audits (facility inspections and process and method audits) to evaluate compliance with internal QMS documents, particularly SOPs and equipment instructions.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 4	4 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Quality Management System
ISO/IEC 17025:2005 Clause	4.2.1
WHO GPPQCL Clause	2.1 & 2.2

Observation Details
The lab's QMS documents are incomplete or do not exist; therefore, the QMS documents do not cover all of the requirements stated in the standards to assure the quality of the testing results.

Objective Evidence
The following are examples of documents that need to be created or updated: 1. Documents that need to be created: a. SOP for cleaning of facilities and equipment b. SOP for control of water utilized for testing c. SOP for method verification 2. Documents that need to be updated: a. Quality Manual: i. Change the scope to ensure the pertinent tests in the medicine QC lab are included. ii. Add an explicit statement indicating compliance with GPPQCL (including the version). This statement should be addressed as a component of the Quality Policy. b. In the sample workflow SOP (PM03-CCP-PR03) add explicit references to the relevant SOPs that detail each stage (ex: add SOP reference for sample receipt, storage, testing, etc…). c. Equipment SOPs that establish acceptable ranges of use. For example, update the equipment SOP for stoves and ensure acceptable ranges of use are explicitly defined. d. Ensure the Memorandum detailing staff responsibilities (and their replacements) is updated and reflects the current responsibilities. e. In the internal audit SOP (PE 02-GC-LABS-P003) ensure the objective and scope of the audits include latest version of WHO GPPQCL. f. Update dissolution equipment records to reflect current compendial recommendations for performance verification testing (PVT). For example, the records for dissolution equipment code EQ-FQ-105 should no longer require the use of salicylic acid tablets as part of the PVT. USP recommends to only perform PVT with prednisone.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Create and/or update SOPs for the relevant activities and ensure all staff is trained prior to their implementations. 2. For the 7 tests to be included in the initial ISO/IEC 17025:2005 accreditation it is recommended to develop a matrix of all the SOPs that are needed to perform the tests in compliance with the standard. This list should include the relevant technical (ex: HPLC, KF, balances, stoves, etc..) and non-technical (ex: internal audit, CAPA, document control, supplier evaluation, etc…) activities. For each SOP the lab can indicate the status of the document (ex: in draft, reviewed and approved, implemented, etc…). This approach will ensure the lab can identify any gaps with their current documents and the requirements of the standards.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 5	5 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Control of Records
ISO/IEC 17025:2005 Clause	4.13.2.1 & 5.6
WHO GPPQCL Clause	4.2 & 13

Observation Details

Systematic deficiencies in the lab's documentary practices, specifically as related to technical records in laboratory notebooks and equipment logbooks. Currently, there are frequent instances of insufficient documentation that does not allow for reproduction of the test under conditions as close as possible to the original test (establish an audit trail).

Objective Evidence

The following are examples deficiencies in the lab's documentary practices:

1. Notebook # 06-2010, which was utilized during the analysis of sample # 19425, did not contain evidence that system suitability was performed during the analysis of the product. As a result it is not possible to confirm if the chromatographic system complies with the method specifications.
2. There is no evidence to ensure internal calibrations are performed while maintaining metrological traceability. The lab is lacking records (either in the lab notebook or the equipment logbook) of the metrological traceability of the materials (balances, buffers, etc….) utilized to perform these calibrations. The following are examples of this nonconformity:
    a. Calibration of balance EQ-FQ-006 from 19 Aug 10
    b. Calibration of balance EQ-FQ-104 on 19 Mar 10
    c. Calibration of pH meter utilized to analyze sample # 19581 as indicated in Notebook # 06-02-2010, P. 373 - 6
3. Notebook # 0602-2010, P. 373 - 6, which was utilized to analyze sample # 19581 had the following issues that do not allow the reproduction of the test under conditions as close as possible to the original test:
    a. Incomplete details for the preparation of the solutions. The following are examples of this nonconformity:
        i. Mobile phase preparation: The notebook states that 2 liters of solution was prepared; however, there is no evidence of what reagents were utilized or their respective proportions.
        ii. Reference standard solution (RS) preparation: The notebook states a specific weight of RS was added to a 25 mL volumetric flask and then 15 mL of EtoH was added. However, there is no more information regarding what reagent was

utilized to bring the solution up to volume.

   b. There is no information regarding the origin (supplier), lot and open/received/expired dates for three reagents (H_3PO_4, ACN & EtOH) utilized in the test.
   c. There is no information regarding the origin (supplier) of the RS utilized in the test.
   d. There is inconsistent data regarding the mobile phase proportions between the HPLC equipment (EQ-FQ-078) logbook entry from 19 Mar 10 and the notebook (P. 374) entry.
4. During the facility inspection, the following deficiencies were identified in the environmental monitoring records of the reference standard storage equipment (camara de almacenamiento de estandares), particularly for equipment code EQ-FQ-107:
   a. All entries recorded without signature of the relevant analyst.
   b. Some entries without the corresponding date of use.
   c. The environmental conditions are recorded using circular recording charts. However, none of the charts indicate what area/equipment the measurements were performed. As a result the lab is not maintaining traceability.
5. The lab does not indicate the date of reception for all lab reagents.
6. A ketoconazole reference standard (lot KT 17045 K4C) was found with no information regarding the lot number on the label and the lab was not able to provide the relevant documents (CoA) for the standard.
7. There is no records for the preparation of the following reagents:
   a. 4 N HNO_3 prepared on 21 Jun 6
   b. 4.8 N HCl prepared on 17 Jun 10.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Update the lab notebook revision SOP and place emphasis on ensuring the notebook review process is more rigorous and can capture any missing data/information. A more stringent review will allow staff to identify any missing data and/or mistakes and ensure there is sufficient information to allow the tests to be repeated under conditions as close as possible to the original test.
2. Track mistakes during all revision processes (notebook, final report and COA) and all internal/external audits. This will help identify recurring mistakes. Use this data to re-train or develop new training activities to remediate and prevent recurring mistakes.
3. Retrain staff on use of notebook SOP to ensure it is clear to all analysts the need to provide sufficient information to allow the tests to be repeated under conditions as close as possible to the original test.

Suggested Timeline

Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 6	6 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Test Methods
ISO/IEC 17025:2005 Clause	5.4.1 & 5.4.2
WHO GPPQCL Clause	16.5 & 17.3

Observation Details

Deviations made to methods without proper justification, documentation and approval by client.

Objective Evidence

Notebook # 0602-2010, P. 373 - 6 provides evidence that the method utilized to analyze sample # 19581 contained deviations that would require revalidation of the method. The following deviations were not justified, documented or approved by the client.

1. The method requires the use of a mobile phase with the following composition: 55% EtOH adjusted with H_3PO_4 to pH ~ 2.8 and 45% ACN. The method utilized was a USP method, which requires compliance with the Chromatography General Chapter <621>. <621> states, "The following adjustment limits apply to minor components of the mobile phase (specified at 50% or less). The amount(s) of these component(s) can be adjusted by ±30% relative." In this case the acceptable range for the minor component (ACN) was 31.5 - 58.5%. The analyst utilized a mobile phase with the following composition: 35% EtOH adjusted with H_3PO_4 to pH ~ 2.8 and 65% ACN. Therefore, the analyst performed unacceptable deviations to the minor component in mobile phase.
2. The method requires filtering of the mobile phase with a 0.22 um filter. The analyst utilized a 0.45 um filter.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Implement Corrective Action # 5, with particular emphasis on ensuring the lab notebook review process is more rigorous to capture any mistakes performed by the analysts and thus ensure any deviations are justified, well documented and approved by the customer.

Suggested Timeline

Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 7	7 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Accommodations (Premises)
ISO/IEC 17025:2005 Clause	5.3.2 - 4
WHO GPPQCL Clause	7.3 & 7.7

Observation Details

The testing environment (infrastructure), particularly in the microbiology laboratory, is not adequate for use and could potentially affect the quality of the results.

Objective Evidence

The laboratory is performing sterility testing and microbiological control in the same area. As a result it is possible to contaminate samples and the results of tests can be compromised.

The following are minor observations that can be easily remediated:

1. In the standard and reagent storage area there is a fume hood that is exposed to a window that is not covered by glass and there are overhead lights that do not contain covers and can easily break.
2. In the sample storage area the paint is peeling and there are yellow (humidity?) spots on the roof.
3. In the female restroom in the first floor the paint is peeling, the hand blower does not work and there are loose cables.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Explore possibilities of developing infrastructure to perform sterility testing and microbiological control in different areas.
2. Improve housekeeping procedures to ensure cosmetic issues with the building infrastructure are addressed.

Suggested Timeline

Address this nonconformity within 1 – 6 months.

Reference Information	
Observation # 8	8 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Equipment
ISO/IEC 17025:2005 Clause	5.5.2, 5.5.5 & 5.5.8
WHO GPPQCL Clause	8.3, 12.2 – 6 & 12.8

Observation Details

The equipment, and the corresponding records, utilized in the lab do not comply with the requirements of the standards.

Objective Evidence

Equipment nonconformities are categorized by area:

1. Use of equipment outside of the corresponding maintenance/calibration dates:
    a. The lab utilized a balance (code: EQ-FQ-0006) three times once the annual calibration had expired. The equipment records (in form PA06-GM-602-F010) states that calibrations are to be performed annually. The two most recent calibrations were performed on 26 May 09 and 13 Aug 10. The calibration performed in 2009 expired in May 2010. The equipment logbook indicated use of the balance after May 2010 and before 13 Aug 10 three times (02, 06 & 10 Jun 10).
    b. The lab's only distiller was marked as being out of service since 16 Jun 09 and there are records (in the equipment logbook) indicating its use on 06 Oct 10
    c. An HPTLC (code: EQ-FQ-076) was marked as being out of service since 01 Oct 10 and there are records (in the equipment logbook) indicating its use on 04 Oct 10
    d. A spectrophotometer (code: EQ-FQ-025) was marked as being out of service since 29 Aug 10 and there are records (in the equipment logbook) indicating its use on 01 Oct 10
2. Lack of adequate equipment labeling. The following are the main deficiencies:
    a. Use of equipment that do not contain individual identification number/code:
        i. Thermometer used to monitor temperature inside refrigerator, code, EQ-MB-018
        ii. Thermometer used to monitor temperature inside oven, internal INVIMA code 04826
    b. Use of equipment that are not labeled with the corresponding calibration status:
        i. Data-logger located in the simple storage areas, code EQ-PO-106
        ii. Data-logger located in the reference standard and reagent storage area, code EQ-FQ-084
        iii. Thermometer used to monitor temperature inside refrigerator code, EQ-MB-018
        iv. Balance, internal INVIMA code 06259
    c. Use of equipment that are not labeled with the corresponding recalibration due date:
        i. Controlled environment chamber used to store reference standards, code EQ-FQ-107

ii. Oven with capacity to create a vacuum, code EQ-FQ-094
iii. Balance, code EQ-FQ-007

3. Equipment records do not comply with the requirements of the standard. The following are the main deficiencies:
    a. There are no records for the use and handling of equipment:
        i. Since 03 Sep 10 there are no records of the use of any equipment in the microbiology lab. Staff indicated they are using the equipment but not recording their use.
        ii. Monthly cleaning/maintenance of equipment (as indicated in the equipment overview record – hoja de vida):
            1. Water purifier, code EQ-FQ-044
            2. HPLC, code EQ-FQ-075
    b. Equipment that are out of service and are not clearly marked:
        i. Freezer, code EQ-FQ-038
        ii. Thermometer used to monitor the temperature in oven, code EQ-FQ-053
        iii. Viscometer, code EQ-FQ-056
    c. Presence of incomplete and/or incorrect equipment records:
        i. The record for approval and verification of qualification for dissolution apparatus, code EQ-FQ-105, did not contain the signatures of the respective staff.
        ii. Records of the qualification of the dissolution equipment, code EQ-FQ-105, did not contain signatures by the corresponding service technicians.
        iii. The label on the balance, internal INVIMA code 02351, contained an incorrect re-calibration due date. The label sates the calibration is due in Jun 10; however this is incorrect as the calibration was performed on 26 Dec 09 and the equipment requires annual maintenance.
    d. Equipment do not contain overview records:
        i. The data-logger located in the sample storage area, code EQ-PO-106
        ii. Microscope located in the Chemistry lab
    e. Balances are utilized without the aid of an anti-vibration surface. As a result the equipment could potentially produce sub-optimal and not trustworthy measurements.
4. Use of volumetric glassware without calibrating and/or verifying if they meet the appropriate specifications.
5. Equipment are not properly qualified and/or verified prior to use.
    a. All of the incubators and baths in the microbiology lab have not been qualified to ensure the temperature readings are reliable.
    b. All of the balances in the microbiology lab are not checked on a daily basis and the lab does not have evidence to justify performing checks with less frequency.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Identify all equipment (including volumetric glassware) whose calibration/maintenance dates have expired (or will shortly expire) and/or require calibration. 2. Ensure all equipment is adequately labeled to prevent the use of equipment outside of valid calibration/maintenance dates. 3. Ensure all staff clearly understand the importance of the following: a. Not utilizing equipment that is marked as out of service and/or has an expired calibration/maintenance status. b. Recording all use of equipment, where appropriate, to ensure adequate records are available. 4. Update the equipment maintenance and calibration program to ensure logistical barriers regarding programming vendor visits are adequately captured in the program. a. If the lab identifies issues with specific equipment it is recommended to update the maintenance and calibration program and/or the equipment SOP to incorporate internal procedures that ensure equipment performance is apt for its intended use. For example, the lab could perform internal performance qualification of Dissolution testers via Performance Verification Testing (see Dissolution Toolkit: http://www.usp.org/pdf/EN/dissolutionProcedureToolkit2010-03.pdf). 5. It is recommended to develop an overview (index) of the major activities (dates of arrival, qualification, put in use, maintenance, moves, out of order, etc…) for each equipment. This will allow the lab to ensure all equipment records are updated and complete. a. As a first step, the lab can perform this exercise for all of the equipment that is relevant for the 7 tests to be included in the initial ISO/IEC 17025:2005 accreditation. 6. Explore the possibility of obtaining anti-vibration surfaces for balances, particularly for measurements that require optimal equipment performance (high level of accuracy). 7. Ensure maintenance/calibration/qualification records (including equipment labels) provided by service technicians meet the requirements of the lab. 8. Update the SOP for use of balances in the microbiology lab and ensure daily checks are performed to ensure the equipment is adequate for use. 9. During facility inspections and process audits, the internal auditor should pay particular attention to the calibration/maintenance status of equipment.

Suggested Timeline
Address this nonconformity within 2 – 5 months.

Reference Information	
Observation # 9	9 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Uncertainty of Measurement
ISO/IEC 17025:2005 Clause	5.4.6.1-3
WHO GPPQCL Clause	18.10

Observation Details
The lab cannot provide an estimated uncertainty of measurement for any of the tests performed.

Objective Evidence
For the majority of tests the lab has sufficient information to establish metrological tractability; however, the lab does not have procedures for calculating the respective estimated uncertainty of measurement.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. The lab should develop a procedure for calculating uncertainty associated with the tests carried out in the lab. This is a complex process and the lab should evaluate the necessary resources needed to implement the appropriate procedure and decide if this activity should be a top priority. If the lab has the necessary resources, PQM recommends the following :
    a. Begin to develop an uncertainty budget for three key tests (i.e.: weights, KF titrations, and HPLC).
    b. Perform a systematic evaluation of all of the factors that contribute to the uncertainty of these three tests. This process will ensure the lab has all of the metrological traceable information that is needed to calculate the estimated uncertainty.
        i. Once the can provide the estimated uncertainty of measurement for these three tests, ensure that these values would allow the lab to calculate the estimated uncertainty of all 7 tests to be included in the initial ISO/IEC 17025:2005 accreditation.
    c. Communicate with PQM and the region's more advanced OMCLs to assist in development of uncertainty budget.

Suggested Timeline
Address this nonconformity within 6 - 9 months.

Reference Information	
Observation # 10	10 of 14
Severity of Non–Conformity	☒ MAJ ☐ MIN ☐ OFI
Area of Evaluation	Monitoring of Environment & Control of Nonconforming Work
ISO/IEC 17025:2005 Clause	4.9 & 5.3.2
WHO GPPQCL Clause	7.3

Observation Details

Environmental conditions (for both storage and testing areas) are improperly monitored to ensure the quality of testing results is not adversely affected. As a result tests are not stopped when environmental conditions outside of acceptable specifications are identified and evaluations of the significance of the environmental deviations are not performed.

Objective Evidence

The following are examples of improper environmental monitoring and/or control and there is no evidence of the lab performing an investigation to evaluate the significance of the environmental deviations:

1. The reference standard storage equipment (camara de almacenamiento de estandares), code EQ-FQ-107, continued to be utilized outside of the acceptable temperature specifications. The equipment it utilized to store materials under "cold" conditions. "Cold" conditions per USP requirements are 2 - 8 °C. During the facility inspection, evidence was found (recorded temperature of 14 °C) that the equipment conditions were outside the specified range.
2. Temperature of the sample storage areas is not continuously monitored. For example there were no records for the temperature of the sample storage area from 01 – 28 Jun 10.
3. Records indicate the freezer INVIMA code 11742 was utilized outside of adequate environmental specifications on 7 – 8 Oct 10.
4. The data-logger located in the storage area of standards and reagents, code EQ-FQ-084, contains records with a maximum temperature of 30 °C. According to the relevant document (PA 06-GM-602-F006), the acceptable range is 21 – 25 °C.

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Ensure there is continuous monitoring of the environmental conditions in the lab.
2. Ensure analysts communicate to the relevant staff when environmental conditions are found to be outside of the established specifications. This will allow the lab to perform an evaluation of the significance of the deviations and determine the appropriate corrective and preventive actions.

Suggested Timeline

Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 11	11 of 14
Severity of Non–Conformity	☐ MAJ ☒ MIN ☐ OFI
Area of Evaluation	Safety
ISO/IEC 17025:2005 Clause	NA
WHO GPPQCL Clause	21.2 & 21.3

Observation Details
Lack of appropriate safety precautions by staff in testing area.

Objective Evidence
The following are examples of inadequate safety procedures: 1. During the facility inspection, several analysts were not using goggles to protect their eyes in testing areas. 2. Waste bottles for HPLC are on the floor without any spillage protection.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Update the lab's safety rules to ensure they address all components of the standard. 2. Ensure all staff follows the lab's safety rules when entering testing areas.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 12	12 of 14
Severity of Non–Conformity	☐ MAJ ☒ MIN ☐ OFI
Area of Evaluation	Supplier Evaluation
ISO/IEC 17025:2005 Clause	4.6.4
WHO GPPQCL Clause	9.2

Observation Details
The labs is not evaluating all suppliers of critical consumables and as a result are utilizing materials that could potentially affect the quality of tests.

Objective Evidence
The lab is not evaluating the supplier of the culture media used for microbiological tests.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Ensure all suppliers of critical consumables are evaluated prior to purchasing and using the obtained materials.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 13	13 of 14
Severity of Non–Conformity	☐ MAJ ☒ MIN ☐ OFI
Area of Evaluation	Storage of Documents & Records
ISO/IEC 17025:2005 Clause	4.13.1.2
WHO GPPQCL Clause	7.5

Observation Details
Documents and records are stored in conditions that could potentially result in their deterioration.

Objective Evidence
In the sample storage areas of both the chemistry and microbiology labs there were documents/records stored on the ground. This practice could lead to documents deteriorating and become unusable.

Suggested Corrective Action
The following actions are recommended to remediate the nonconformity: 1. Ensure all documents are not placed on the ground in storage areas and are placed in shelves and/or cabinets that can prevent their deterioration. 2. During facility inspections, the internal auditor should pay particular attention to this issue.

Suggested Timeline
Address this nonconformity within 1 – 3 months.

Reference Information	
Observation # 14	14 of 14
Severity of Non–Conformity	☐ MAJ ☐ MIN ☒ OFI
Area of Evaluation	Reporting of Results
ISO/IEC 17025:2005 Clause	5.10.2.k & 5.10.2 – Note 2
WHO GPPQCL Clause	18.11

Observation Details

Emission of Certificate of Analysis (CoA – also referred to the analytical test report) that does not contain all of the information as required by the standards.

Objective Evidence

The following are examples deficiencies in the lab's CoA:

1. Missing a statement that clarifies the test results only pertain to the specific product (sample) tested.
2. Missing a statement indicating that any information presented in the CoA cannot be reproduced without prior authorization of the laboratory.
    a. Comment: This issue cannot be included as an observation during an ISO/IEC 17025:2005 assessment as it is included in a note (5.10.2 – Note 2).

Suggested Corrective Action

The following actions are recommended to remediate the nonconformity:

1. Amend the CoA template to include statements similar to the following:
    a. The results contained in this CoA only pertain to the sample tested and should not be utilized to make conclusions about other samples/materials/products.
    b. The contents of this CoA cannot be reproduced without the authorization of INVIMA.

Suggested Timeline

Address this nonconformity within 1 – 3 months.